PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference EDIM/P28643PC	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/02879	International filing date *(day/month/year)* 04.07.2003	Priority date *(day/month/year)* 05.07.2002
International Patent Classification (IPC) or both national classification and IPC C07F15/00		
Applicant THE UNIVERSITY COURT, THE UNIVERSITY OF EDINBURGH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 14 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.01.2004	26.08.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Richter, H Telephone No. +49 89 2399-8539

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/02879

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-27 as originally filed

Claims, Numbers

1-26 received on 13.08.2004 with letter of 13.08.2004

Drawings, Sheets

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-26
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-26
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-24, 26
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Quoted documents:

D1: SHIN, RICHARD Y. C. ET AL: "Arene-Ruthenium Complexes of an Acyclic Thiolate-Thioether and Tridentate Thioether Derivatives Resulting from Ring-Closure Reactions" INORGANIC CHEMISTRY (2003), 42(1), 96-106, XP002259899

D2: BEN AMMAR, HAMED ET AL: "Synthesis of bis-oxazoline-ruthenium(II)-arene complexes. Combined catalytic isomerization and Claisen rearrangement of bis-allyl ether" JOURNAL OF ORGANOMETALLIC CHEMISTRY (2002), 662(1-2), 63-69, XP002259901

D3: CHEN HAIMEI ET AL: "Organometallic ruthenium(II) diamine anticancer complexes: arene-nucleobase stacking and stereospecific hydrogen-bonding in guanine adducts." JOURNAL OF THE AMERICAN CHEMICAL SOCIETY. UNITED STATES 27 MAR 2002, vol. 124, no. 12, 27 March 2002 (2002-03-27), pages 3064-3082, XP002259900 ISSN: 0002-7863

D4: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BELL, MICHAEL N. ET AL: "Carbocyclic complexes incorporating macrocyclic ligands. The synthesis and single crystal x-ray structure of the binuclear species dichlorobis(.eta.-pentamethylcyclopentadie nyl)(1,4,7,10,13,1 6-hexathiacyclooctadecane)dirhodium bis(tetraphenylborate)" XP002259903 retrieved from STN Database accession no. 106:84806

D5: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; BENNETT, MARTIN A. ET AL: "Mono- and bis-(acetylacetonato) complexes of arene-ruthenium(II) and arene-osmium(II): variation of the binding mode of.eta.1-acetylacetonate with the nature of the arene" XP002259904 retrieved from STN Database accession no. 135:371841

D6: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS,

OHIO, US; DAVIES, DAVID L. ET AL: "(Arene)ruthenium Complexes with Bis(oxazolines): Synthesis and Applications as Asymmetric Catalysts for Diels-Alder Reactions" XP002259905 retrieved from STN Database accession no. 135:152944

D7: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; OHNISHI, TAKAFUMI ET AL: "Coordination behavior of ruthenium(II) complexes with alcohol ligand tethered to.eta.6-arene donor" XP002259906 retrieved from STN Database accession no. 131:257682

D8: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; EVERAERE, KATHELYNE ET AL: "(.beta.-Amino alcohol)(arene)ruthenium(II)-catalyzed asymmetric transfer hydrogenation of functionalized ketones - scope, isolation of the catalytic intermediates, and deactivation processes" XP002259907 retrieved from STN Database accession no. 134:295540

D9: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; WOISETSCHLAGER, OLIVER E. ET AL: "Hydrocarbon-bridged metal complexes. Part 49. Coordination chemistry of bis(ferrocenyl)-substituted 1,3-diketonates with ruthenium, rhodium, iridium, and palladium" XP002259908 retrieved from STN Database accession no. 132:308480

D10: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KATHO, AGNES ET AL: "Enantioselective hydride transfer hydrogenation of ketones catalyzed by [(.eta.6-p-cymene)Ru(amino acidato)Cl] and [(.eta.6-p- cymene)Ru(amino acidato)]3(BF4)3 complexes" XP002259909 retrieved from STN Database accession no. 132:222637

D11: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; MIYAKI, Y. ET AL: "Synthesis and reaction of ruthenium(II) complexes containing heteroatom donor (O, N, and P) tethered to.eta.6-arene ring" XP002259910 retrieved from STN Database accession no. 133:135395

D12: FALLER, J. W. ET AL: "Highly enantioselective Diels-Alder catalysis with a chiral ruthenium bisoxazoline complex" JOURNAL OF ORGANOMETALLIC CHEMISTRY (2001), 630(1), 17-22, XP002259902

D13: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; SIMAL, FRANCOIS ET AL: "Ruthenium complexes containing diamine-based ligands as catalysts for insertion of carbenes into O-H bonds of alcohols" XP002259911 retrieved from STN Database accession no. 130:222808

D14: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KUROSAWA, HIDEO ET AL: "Second sphere coordination behavior of aquo and amine ligands bound to a.eta.6-benzeneruthenium(II) cation" XP002259912 retrieved from STN Database accession no. 128:257553

D15: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KUHLWEIN, FRANK ET AL: "Metal complexes of dyes. Part 9. Transition metal complexes of curcumin and derivatives" XP002259913 retrieved from STN Database accession no. 127:228818

D16: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KRAEMER, ROLAND ET AL: "Metal complexes of biologically important ligands. LIII. Chiral half-sandwich complexes of rhodium(III), iridium(III), iridium(I), and ruthenium(II) with.alpha.-amino acid anions" XP002259914 retrieved from STN Database accession no. 112:198744

D17: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; SHELDRICK, W. S. ET AL: "Synthesis and structural characterization of.eta.6- areneruthenium(II) complexes of.alpha.-amino acids with coordinating side chains" XP002259915 retrieved from STN Database accession no. 113:59793

D18: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; GOETZE, H. J. ET AL: "Separation of amino-acidato ruthenium(II) complexes by ion-pair chromatography" XP002259916 retrieved from STN Database accession no. 120:94149

D19: EP-A-0 916 637 (JAPAN SCIENCE AND TECHNOLOGY CORPORATION, JAPAN;NKK CORPORATION; TAKED) 19 May 1999 (1999-05-19)

D20: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS,

OHIO, US; CARMONA, DANIEL ET AL: "Heterobi- and Heterotetranuclear RuRh and RuIr Complexes with 2,2'-Biimidazolate and 2,2'-Bibenzimidazolate Anions as Bridging Ligands" XP002259931 retrieved from STN Database accession no. 122:214225

D21: STERN C ET AL: "The use of macrocyclic and polydentate ligands in ruthenium organometallic chemistry" JOURNAL OF ORGANOMETALLIC CHEMISTRY, ELSEVIER-SEQUOIA S.A. LAUSANNE, CH, vol. 593-594, January 2000 (2000-01), pages 86-95, XP004185686 ISSN: 0022-328X

D22: WO-A-02/02572

D23: WO-A-01/30790

D24: XP009020330; Cremona; Inorg. Chem. 1990, (4), 1463-76

The document D24 was not cited in the international search report. A copy of the document is appended hereto.

1. For the assessment of the present claim 25 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment like present claim 23.

2. The documents D1 and D2 indicated in the search report as P(X)-documents are not considered to be prior art as the date of priority claimed can be allowed for the relevant parts of the present application.

3. The subject-matter of documents D5, D8-D10, D15 and D20 is the subject of the provisos in claim 1. Newly cited document D24; see scheme 1, table 1, and formulas 6 9a, 9b, 15-17 seems to be fully covered by the first disclaimer in claim 1. The documents are so called "accidentally novelty destroying disclosures" as defined by decision **G1/03** (see Headnote 2.1. The subject-matter of which may

be removed from the present application by way of disclaimer. D5, D8-D10, D15 and D20 disclose several examples (see the search report for the details) which fall inside the provisos but there is nowhere in these documents is a reference to the anti-cancer activity of the compounds. Hence, the provisos can be accepted. Consequently, documents D5, D8-D10, D15, D20 and D24 are not pertinent in the question of novelty and inventive step.

4. The limiting factors over D4, D6, D7, D11-D14, and D16-D18 are shown in the enclosure.

5. Compounds shown in chart 1 according to D3 are distinguished from subject-matter of the present application only in the presence of the negative charge on the bidentate ligand Y-L-Y'. Compounds similar to those according to D3 are also disclosed in D22 (see pages 8 and 9) and D23. These patent documents are also cited in the application).

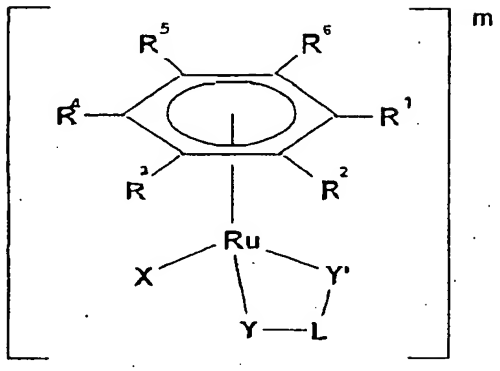
6. The lower charge of the claimed complexes in comparison with the complexes mentioned under item 5. allows them to bind adenine as well as guanine. This is an advantage in treating drug resistent tumor cells.

7. Claims 13-22 lack clarity because the partial phrase in claim 13 "use in medicine" does not distinguish between surgery, therapy and diagnosis. This distinction may be important in the national phase; see Guidelines for examination in the European Patent Office, CIV, 4.2, page 587: the claims are restricted to the substance or composition when presented or packaged for the use. Clearly, such presentation is different when use is for therapy rather than for e.g. diagnosis.

8. The description (see inter alia page 5) is not in conformity with the claims as required by Rule 5.1(a)(iii) PCT.

CLAIMS

1. Ruthenium(II) compound of formula(I) :



(I)

wherein: R^1, R^2, R^3, R^4, R^5 and R^6 independently represent H, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, hydroxy$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, halo, CO_2R^7, $CONR^8R^9$, COR^{10}, SO_3H, $SO_2NR^{11}R^{12}$, aryloxy, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, -N=N-R^{13}, $NR^{14}R^{15}$, aryl or aralkyl, which latter two groups are optionally substituted on the aromatic ring by one or more groups independently selected from $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, hydroxy$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, aryl, aralkyl, halo, CO_2R^{7a}, $CONR^{8a}R^{9a}$, COR^{10a}, SO_3G, $SO_2NR^{11a}R^{12a}$, aryloxy, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, -N=N-R^{13a}, $NR^{14a}R^{15a}$, or R^1 and R^2 together with the ring to which they are bound represent a saturated or unsaturated carbocyclic or heterocyclic group containing up to three 3-to 8-membered carbocyclic or heterocyclic rings, wherein each carbocyclic or heterocyclic ring may be fused to one or more other carbocyclic or heterocyclic rings, and wherein each of the rings may be optionally substituted by one or more groups independently selected from $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, hydroxy$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, aryl, aralkyl, halo, CO_2R^{7b}, $CONR^{8b}R^{9b}$, COR^{10b}, SO_3G', $SO_2NR^{11b}R^{12b}$, aryloxy, $(C_1$-$C_6)$alkylthio, -N=N-R^{13b}, $NR^{14b}R^{15b}$ or $(C_1$-$C_6)$alkoxy;

R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{7a}, R^{8a}, R^{9a}, R^{10a}, R^{11a}, R^{12a}, R^{13a}, R^{14a}, R^{15a}, R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, and R^{15b} are independently selected from H, (C_1-C_6)alkyl, aryl or aralkyl;

X is a neutral or negatively charged O-, N- or S-donor ligand or halo;

G and G' are independently selected from alkali metals, aryl, aralkyl and (C_1-C_6) alkyl;

Y-L-Y' is a bidentate ligand bearing a negative charge with a proportion of the charge on both Y and Y', Y and Y' are independently selected from O, S or NR^{16}, wherein R^{16} is H, (C_1-C_6) alkyl, aryl or aralkyl, and L is a group linking Y and Y' and comprises one or more groups selected from (C_1-C_6) alkylene, (C_1-C_6) alkenylene, (C_1-C_6) alkynylene, arylene, aralkylene, alkarylene, each of said latter six groups being optionally substituted, ferrocenylene, Se, Se-Se, S-S, N=N and C=O;

m is -1, 0 or +1 and the compound comprises a counterion when m is -1 or +1;

the compound of formula (I) optionally being in the form of a dimer in which two L groups are linked either directly or through a group comprising one or more of (C_1-C_6) alkylene, (C_1-C_6) alkenylene, arylene, aralkylene, alkarylene, Se, Se-Se, S-S, N=N and C=O or in which L bears two Y groups and two Y' groups;

with the provisos that:

when Y-L-Y' is $(CH_3C(O)CHC(O)CH_3)^-$, X is halo or an N-donor ligand, R^1, R^2, R^3, R^4, R^5 and R^6 together with the ring to which they are bound do not represent 4-isopropyl-1-methylbenzene;

when Y-L-Y' is $(CH_3C(O)CHC(O)CH_3)^-$ and X is chloro, $(CH_3)_2SO$, CH_3CN, pyridine or $(CH_3C(O)CHC(O)CH_3)^-$: R^1, R^2, R^3, R^4, R^5 and R^6 are not all H or all methyl; R^1, R^3 and R^5 are not all H when R^2, R^4 and R^6 are all methyl; and R^2, R^4 and R^6 are not all H when R^1, R^3 and R^5 are all methyl;

when Y-L-Y' is $(CF_3C(O)CHC(O)CHF_3)^-$ and X is chloro, R^1, R^2, R^3, R^4, R^5 and R^6 are not all H or all methyl; R^1, R^3 and R^5 are not all H when R^2, R^4 and

R^6 are all methyl; and R^2, R^4 and R^6 are not all H when R^1, R^3 and R^5 are all methyl;

when Y-L-Y' is $(CF_3C(O)CHC(O)OEt)^-$ and X is chloro, R^1, R^2, R^3, R^4, R^5 and R^6 together with the ring to which they are bound do not represent 4-isopropyl-1-methylbenzene;

when Y-L-Y' is $((ferrocenylene)C(O)CHC(O)(ferrocenylene))^-$ and X is chloro, R^1, R^2, R^3, R^4, R^5 and R^6 together with the ring to which they are bound do not represent 4-isopropyl-1-methylbenzene;

when R^1, R^2, R^3, R^4, R^5 and R^6 together with the ring to which they are bound represent 4-isopropyl-1-methylbenzene and X is chloro, Y-L-Y' is neither $(4\text{-}OH\text{-}5\text{-}OCH_3\text{-}PhCHCHC(O)CHC(O)CHCH\text{-}4\text{-}OH\text{-}5\text{-}OCH_3\text{-}Ph)^-$, $(4\text{-}OCH_3\text{-}5\text{-}OCH_3\text{-}PhCHCHC(O)C(CH_3)C(O)CHCH\text{-}4\text{-}OCH_3\text{-}5\text{-}OCH_3\text{-}Ph)^-$, $(4\text{-}COOCH_3\text{-}5\text{-}OCH_3\text{-}PhCHCHC(O)CHC(O)CHCH\text{-}4\text{-}COOCH_3\text{-}5\text{-}OCH_3\text{-}Ph)^-$, $(4\text{-}OH\text{-}5\text{-}H\text{-}PhCHCHC(O)CHC(O)CHCH\text{-}4\text{-}OH\text{-}5\text{-}H\text{-}Ph)^-$ nor $(4\text{-}OCH_3\text{-}5\text{-}OCH_3\text{-}PhCHCHC(O)CHC(O)CHCH\text{-}4\text{-}OCH_3\text{-}5\text{-}OCH_3\text{-}Ph)^-$.

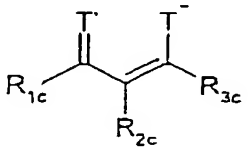
2. Compound as claimed in Claim 1, wherein R^1, R^2, R^3, R^4, R^5 and R^6 are independently selected from H, $(C_1\text{-}C_6)$ alkyl and phenyl or R^1 and R^2 together with the ring to which they are bound represent anthracene or a hydrogenated derivative of anthracene, said phenyl and anthracene or a hydrogenated derivative of anthracene group being optionally substituted by one or more groups independently selected from $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$alkynyl, hydroxy$(C_1\text{-}C_6)$alkyl, amino$(C_1\text{-}C_6)$alkyl, phenyl, benzyl, halo, carboxyl, $CO_2(C_1\text{-}C_6)$alkyl, $CONH_2$, COH, $CO(C_1\text{-}C_6)$alkyl, SO_3H, SO_2NH_2, phenoxy, $(C_1\text{-}C_6)$alkylthio, NH_2 or $(C_1\text{-}C_6)$ alkoxy.

3. Compound as claimed in Claim 1 or Claim 2, wherein m is 0.

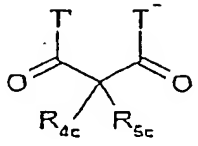
4. Compound as claimed in any one of Claims 1 to 3, wherein X is halo or

CH_3CN.

5. Compound as claimed in any one of Claims 1 to 4, wherein Y-L-Y' is selected from ligands of formulae (II) to (X):



(II)



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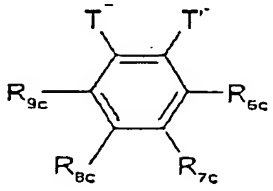

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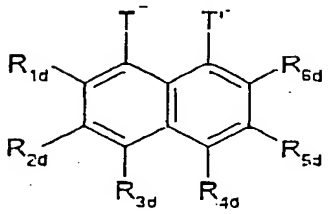

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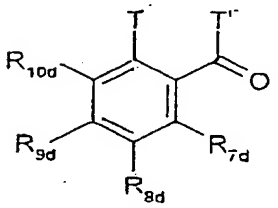

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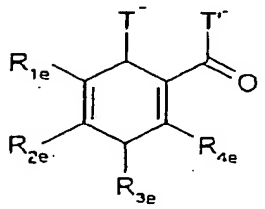

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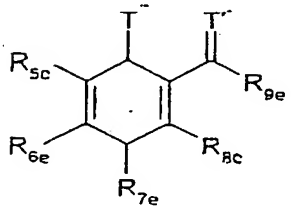
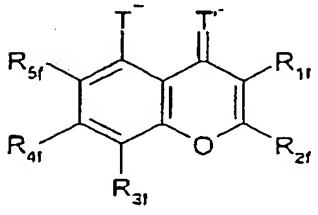
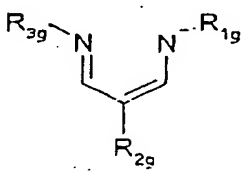


(VIII)



(IX)



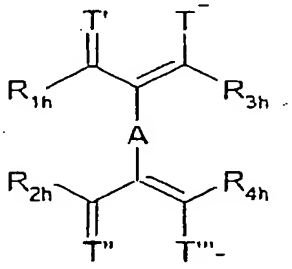
(X)

wherein T and T' are independently selected from O and S,

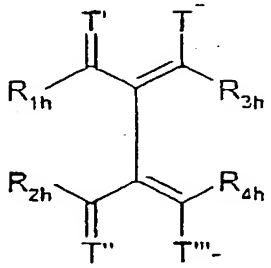
R_{1g} and R_{3g} are independently H, (C_1-C_6) alkyl, aryl or aralkyl,

R_{1c} to R_{5f} and R_{2g} are independently H, (C_1-C_6)alkyl, aryl, aralkyl, wherein the latter two groups and the corresponding groups for R_{1g} and R_{3g} are optionally substituted by one or more groups independently selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, aryl, aralkyl, halo, CO_2R^{7b}, $CONR^{8b}R^{9b}$, COR^{10b}, SO_3G', $SO_2NR^{11b}R^{12b}$, aryloxy, (C_1-C_6)alkylthio, -N=N-R^{13b}, $NR^{14b}R^{15b}$ or (C_1- C_6)alkoxy, wherein R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, and R^{15b} are as defined in Claim 1.

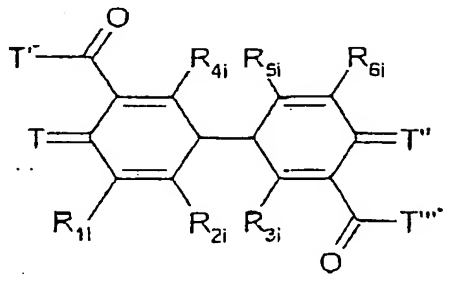
6. Compound as claimed in any one of Claims 1 to 4, wherein Y-L-Y' is selected from:



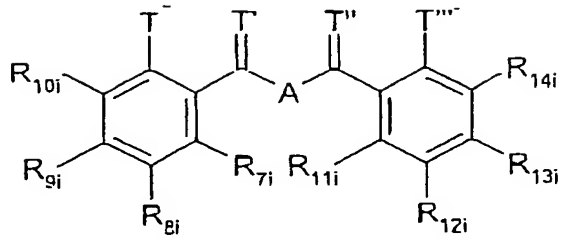
(XI)



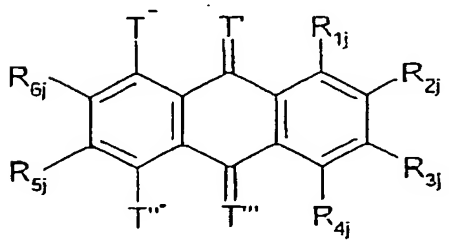
(XII)



(XIII)



(XIV)



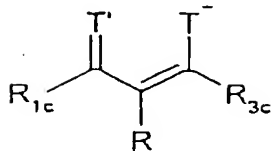
(XV)

wherein T, T', T" and T"' are independently selected from O and S,

A comprises one or more groups selected from (C_1-C_6)alkylene, (C_1-C_6)alkenylene, (C_1-C_6) alkynylene, arylene, aralkylene, alkarylene, ferrocenylene, Se, Se-Se, S-S, N=N and C=O

and R_{1h} to R_{6j} are independently H, (C_1-C_6)alkyl, aryl, aralkyl, wherein the latter two groups are optionally substituted by one or more groups independently selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, aryl, aralkyl, halo, CO_2R^{7b}, $CONR^{8b}R^{9b}$, COR^{10b}, SO_3G', $SO_2NR^{11b}R^{12b}$, aryloxy, (C_1-C_6)alkylthio, -N=N-R^{13b}, $NR^{14b}R^{15b}$ or (C_1- C_6)alkoxy, wherein R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, and R^{15b} are as defined in Claim 1.

7. Compound as claimed in any one of Claims 1 to 4, wherein Y-L-Y' is:



wherein T and T' are independently O and S, and R, R_{1c}, and R_{3c} are independently H, (C_1-C_6)alkyl, aryl, aralkyl, wherein the latter two groups are optionally substituted by one or more groups independently selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, aryl, aralkyl, halo, CO_2R^{7b}, $CONR^{8b}R^{9b}$, COR^{10b}, SO_3G', $SO_2NR^{11b}R^{12b}$, aryloxy, (C_1-C_6)alkylthio, -N=N-R^{13b}, $NR^{14b}R^{15b}$ or (C_1-C_6)alkoxy, wherein R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, and R^{15b} are as defined in Claim 1.

8. Compound as claimed in claim 7, wherein one of R^1, R^2, R^3, R^4, R^5 and R^6 is phenyl and the other groups are H.

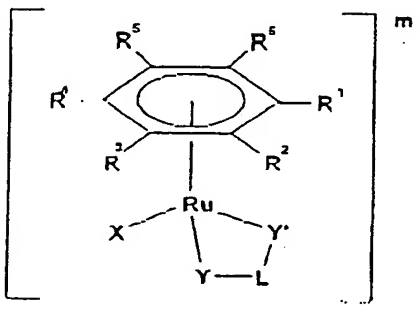
9. Compound as claimed in Claim 7 or Claim 8, wherein T and T' are both O, R is H or (C_1-C_6) alkyl and R_{1c} and R_{3c} are independently (C_1-C_6)alkyl or phenyl, said phenyl optionally substituted by (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6) alkyl, halo, carboxyl, CO_2(C_1-C_6)alkyl, $CONH_2$, COH, CO(C_1-C_6)alkyl, SO_3H, SO_2NH_2, phenoxy, (C_1-C_6) alkylthio, NH_2 or (C_1-C_6)alkoxy.

10. Compound as claimed in claim 9, wherein R_{1c} and R_{3c} are independently phenyl, said phenyl optionally substituted by (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6) alkyl, halo, carboxyl, CO_2(C_1-C_6)alkyl, $CONH_2$, COH, CO(C_1-C_6)alkyl, SO_3H, SO_2NH_2, phenoxy, (C_1-C_6) alkylthio, NH_2 or (C_1-C_6)alkoxy.

11. Compound as claimed in claim 9, wherein R is H and R_{1c} and R_{3c} are independently (C_1-C_6)alkyl or phenyl.

12. Compound as claimed in any one of Claims 1 to 9, wherein Y and Y' are both O.

13. Ruthenium(II) compound of formula(I) :



(I)

for use in medicine, wherein:

R^1, R^2, R^3, R^4, R^5 and R^6 independently represent H, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, halo, CO_2R^7, $CONR^8R^9$, COR^{10}, SO_3H, $SO_2NR^{11}R^{12}$, aryloxy, (C_1-C_6)alkoxy, (C_1-C_6)alkylthio, $-N=N-R^{13}$, $NR^{14}R^{15}$, aryl or aralkyl, which latter two groups are optionally substituted on the aromatic ring by one or more groups independently selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, aryl, aralkyl, halo, CO_2R^{7a}, $CONR^{8a}R^{9a}$, COR^{10a}, SO_3G, $SO_2NR^{11a}R^{12a}$, aryloxy, (C_1-C_6)alkoxy, (C_1-C_6)alkylthio, $-N=N-R^{13a}$, $NR^{14a}R^{15a}$, or R^1 and R^2 together with the ring to which they are bound represent a saturated or unsaturated carbocyclic or heterocyclic group containing up to three 3-to 8-membered carbocyclic or heterocyclic rings, wherein each carbocyclic or heterocyclic ring may be fused to one or more other carbocyclic or heterocyclic rings, and wherein each of the

rings may be optionally substituted by one or more groups independently selected from $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, hydroxy$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, aryl, aralkyl, halo, CO_2R^{7b}, $CONR^{8b}R^{9b}$, COR^{10b}, SO_3G', $SO_2NR^{11b}R^{12b}$, aryloxy, $(C_1$-$C_6)$alkylthio, $-N=N-R^{13b}$, $NR^{14b}R^{15b}$ or $(C_1$-$C_6)$alkoxy;

R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{7a}, R^{8a}, R^{9a}, R^{10a}, R^{11a}, R^{12a}, R^{13a}, R^{14a}, R^{15a}, R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, and R^{15b} are independently selected from H, $(C_1$-$C_6)$alkyl, aryl or aralkyl;

X is a neutral or negatively charged O-, N- or S-donor ligand or halo;

G and G' are independently selected from alkali metals, aryl, aralkyl and $(C_1$-$C_6)$ alkyl;

Y-L-Y' is a bidentate ligand bearing a negative charge with a proportion of the charge on both Y and Y', Y and Y' are independently selected from O, S or NR^{16}, wherein R^{16} is H, $(C_1$-$C_6)$ alkyl, aryl or aralkyl, and L is a group linking Y and Y' and comprises one or more groups selected from $(C_1$-$C_6)$ alkylene, $(C_1$-$C_6)$ alkenylene, $(C_1$-$C_6)$ alkynylene, arylene, aralkylene, alkarylene, each of said latter six groups being optionally substituted, ferrocenylene, Se, Se-Se, S-S, N=N and C=O;

m is -1, 0 or +1 and the compound comprises a counterion when m is -1 or +1;

the compound of formula (I) optionally being in the form of a dimer in which two L groups are linked either directly or through a group comprising one or more of $(C_1$-$C_6)$ alkylene, $(C_1$-$C_6)$ alkenylene, arylene, aralkylene, alkarylene, Se, Se-Se, S-S, N=N and C=O or in which L bears two Y groups and two Y' groups.

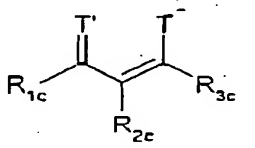
14. Compound as claimed in Claim 13, wherein R^1, R^2, R^3, R^4, R^5 and R^6 are independently selected from H, $(C_1$-$C_6)$ alkyl and phenyl or R^1 and R^2 together with the ring to which they are bound represent anthracene or a hydrogenated derivative of anthracene, said phenyl and anthracene or a

hydrogenated derivative of anthracene group being optionally substituted by one or more groups independently selected from $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$ alkenyl, $(C_2$-$C_6)$alkynyl, hydroxy$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, phenyl, benzyl, halo, carboxyl, $CO_2(C_1$-$C_6)$alkyl, $CONH_2$, COH, $CO(C_1$-$C_6)$alkyl, SO_3H, SO_2NH_2, phenoxy, $(C_1$-$C_6)$alkylthio, NH_2 or $(C_1$-$C_6)$ alkoxy.

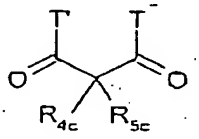
15. Compound as claimed in Claim 13 or Claim 14, wherein m is 0.

16. Compound as claimed in any one of Claims 13 to 15, wherein X is halo or CH_3CN.

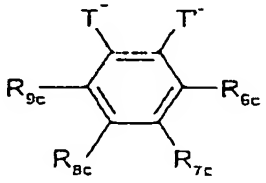
17. Compound as claimed in any one of Claims 13 to 16, wherein Y-L-Y' is selected from ligands of formulae (II) to (X):



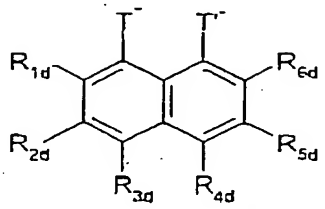
(II)



(III)



(IV)



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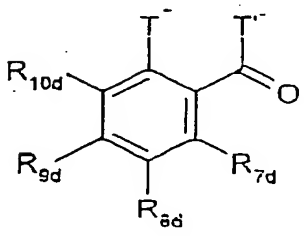
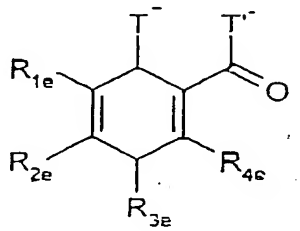
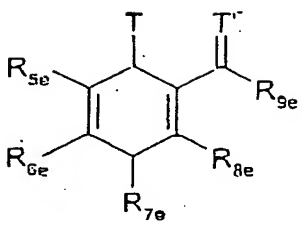


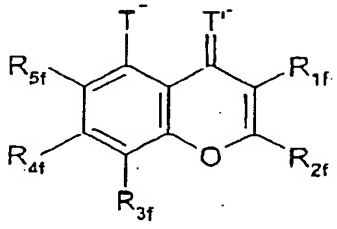
(VI)



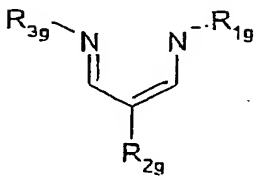
(VII)



(VIII)



(IX)



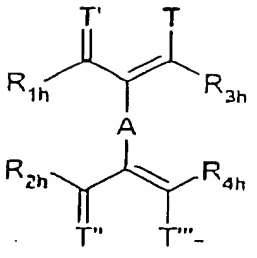
(X)

wherein T and T' are independently selected from O and S,

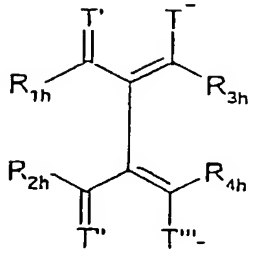
R_{1g} and R_{3g} are independently H, (C_1-C_6) alkyl, aryl or aralkyl,

R_{1c} to R_{5f} and R_{2g} are independently H, (C_1-C_6)alkyl, aryl, aralkyl, wherein the latter two groups and the corresponding groups for R_{1g} and R_{3g} are optionally substituted by one or more groups independently selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, aryl, aralkyl, halo, CO_2R^{7b}, $CONR^{8b}R^{9b}$, COR^{10b}, SO_3G', $SO_2NR^{11b}R^{12b}$, aryloxy, (C_1-C_6)alkylthio, -N=N-R^{13b}, $NR^{14b}R^{15b}$ or (C_1- C_6)alkoxy, wherein R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, and R^{15b} are as defined in Claim 13.

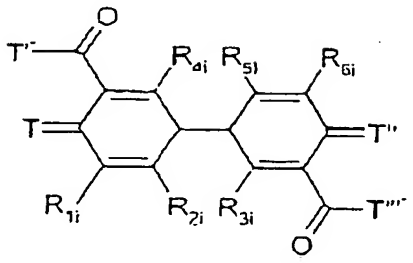
18. Compound as claimed in any one of Claims 13 to 16, wherein Y-L-Y' is selected from:



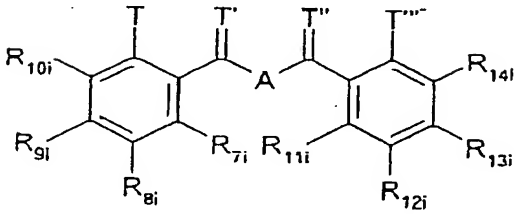
(XI)



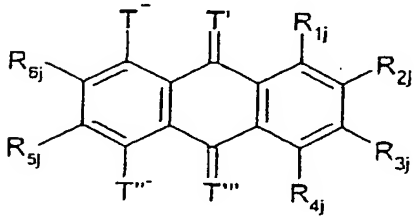
(XII)



(XIII)



(XIV)



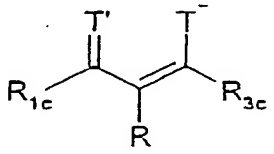
(XV)

wherein T, T', T" and T"' are independently selected from O and S,

A comprises one or more groups selected from (C_1-C_6)alkylene, (C_1-C_6)alkenylene, (C_1-C_6) alkynylene, arylene, aralkylene, alkarylene, ferrocenylene, Se, Se-Se, S-S, N=N and C=O

and R_{1h} to R_{6j} are independently H, (C_1-C_6)alkyl, aryl, aralkyl, wherein the latter two groups are optionally substituted by one or more groups independently selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, aryl, aralkyl, halo, CO_2R^{7b}, $CONR^{8b}R^{9b}$, COR^{10b}, SO_3G', $SO_2NR^{11b}R^{12b}$, aryloxy, (C_1-C_6)alkylthio, -N=N-R^{13b}, $NR^{14b}R^{15b}$ or (C_1- C_6)alkoxy, wherein R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, and R^{15b} are as defined in Claim 13.

19. Compound as claimed in any one of Claims 13 to 16, wherein Y-L-Y' is:



wherein T and T' are independently O and S, and R, R_{1c}, and R_{3c} are independently H, (C_1-C_6)alkyl, aryl, aralkyl, wherein the latter two groups are optionally substituted by one or more groups independently selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, aryl, aralkyl, halo, CO_2R^{7b}, $CONR^{8b}R^{9b}$, COR^{10b}, SO_3G', $SO_2NR^{11b}R^{12b}$, aryloxy, (C_1-C_6)alkylthio, -N=N-R^{13b}, $NR^{14b}R^{15b}$ or (C_1-C_6)alkoxy, wherein R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{11b}, R^{12b}, R^{13b}, R^{14b}, and R^{15b} are as defined in Claim 13.

20. Compound as claimed in Claim 19, wherein T and T' are both O, R is H or (C_1-C_6) alkyl and R_{1c} and R_{3c} are independently (C_1-C_6)alkyl or phenyl, said

phenyl optionally substituted by (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6) alkyl, halo, carboxyl, CO_2(C_1-C_6)alkyl, $CONH_2$, COH, CO(C_1-C_6)alkyl, SO_3H, SO_2NH_2, phenoxy, (C_1-C_6) alkylthio, NH_2 or (C_1-C_6)alkoxy.

21. Compound as claimed in claim 20, wherein R is H and R_{1c} and R_{3c} are independently (C_1-C_6)alkyl or phenyl.

22. Compound as claimed in any one of Claims 13 to 21, wherein Y and Y' are both O.

23. Use of a compound of formula (I) according to any one of Claims 13 to 22, in the manufacture of a medicament for the treatment and/or prevention of cancer.

24. Pharmaceutical composition comprising a compound of formula (I) according to any one of Claims 13 to 21, together with one or more pharmaceutically acceptable excipients.

25. A method of treating and/or preventing cancer which comprises administering to a subject a therapeutically effective amount of a compound of formula (I) according to any one of Claims 13 to 21 without the provisos, or a composition of Claim 24.

26. Process for preparing the compound of any one of Claims 1 to 12 which comprises the reaction of a compound of formula [(η^6-$C_6(R^1)(R^2)(R^3)(R^4)(R^5)(R^6)$) RuX_2], optionally in the form of a dimer, with Y-L-Y, in a suitable solvent for the reaction, wherein R^1, R^2, R^3, R^4, R^5, R^6, X, Y, Y' and L are as defined in Claim 1.